Callosal Neglect

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**Background:** According to the interhemispheric inhibition model of neglect, the uninjured hemisphere inhibits (via the corpus callosum) the injured hemisphere but the injured hemisphere can no longer inhibit the opposite hemisphere, which becomes hyperactive and produces an ipsilesional attentional bias. Alternatively, according to the compensation hypothesis, the uninjured hemisphere helps compensate for the damaged hemisphere, which is impaired in directing attention to contralateral stimuli. If the inhibition model of neglect is correct, callosal disconnection should reduce neglect. If the compensation model is correct, however, it may increase or induce neglect.

**Patient:** A 32-year-old woman, at age 14 years, developed a right frontal astrocytoma and was treated with surgery and radiation but had a cardiopulmonary arrest secondary to aspiration. Subsequent imaging studies revealed damage to the frontal, parietal, and occipital regions of the right hemisphere and damage to the temporal region of the left hemisphere. After discharge, she was able to return to school and drive a car, without any evidence of neglect. About 10 years later, she developed complex partial and atonic seizures that were multifocal and medically intractable. She underwent a complete section of her corpus callosum at age 31 years.

**Results:** One year after the callosal section, she demonstrated (1) diminished spontaneous saccades to the left, hypometric leftward saccades, and left gaze impersistence; (2) left arm hemispatial limb akinesia; (3) unilateral spatial neglect; and (4) motor and cognitive impersistence.

**Conclusion:** In patients with right hemisphere injury, callosal section may induce or enhance motor-intentional deficits and hemispatial neglect.

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**REPORT OF A CASE**

A 32-year-old, right-handed woman developed headaches at the age of 14 years. An evaluation revealed a right frontal tu-
The tumor was a grade 3 astrocytoma. In addition to surgery, the tumor was treated with radiation. While in the hospital for treatment of this tumor, she had a cardiopulmonary arrest secondary to aspiration that may have been related to a seizure. Computed tomography (CT) at this time revealed damage to the frontal, parietal, and occipital regions of the right hemisphere. There was also some injury to the temporal lobe of the left hemisphere. Subsequent magnetic resonance imaging (MRI) confirmed these findings. Although she had a transient left hemiparesis, the only residual sign from the tumor, surgery, radiation, and cardiopulmonary arrest was a left hemianopsia.

After discharge, she was able to return to school and drive a car, but did have some difficulty with reading. At the age of 24 or 25 years, she developed seizures. Initially, these were simple partial gelastic seizures but progressed to complex partial and atonic seizures. The complex partial seizures started with head turning to the right. The atonic seizures were associated with frequent falls with head injuries. She developed several subdural hematomas that required drainage. Her seizures were frequent (about 4 per day) and intractable despite the use of a variety of anticonvulsant medications. Inpatient electroencephalogram (EEG)/video monitoring, on 4 occasions between 1993 and 1999 showed spike discharges that variably were localized to the right frontocentral region, the right temporal region, or the left frontal regions. Her last EEG, taken just before surgery, revealed diffuse ictal events with an electrodecremental response but without lateralizing or localizing features. Intracranial monitoring was not performed because she had multiple types of seizure and multiple areas of damage. The patient and her family did not want a trial with vagal stimulation. Because her seizures could not be managed with medications and EEG monitoring did not reveal a primary epileptic focus that could be resected with a good probability of success, she underwent a complete section of her corpus callosum on October 25, 1999.

Following her surgery, and with a regimen of clonazepam, 3 mg/d, and topiramate, 350 mg/d, her epilepsy improved dramatically, with infrequent 2-second lapses that were not associated with falls. Postoperatively, however, she was not using her left arm and was neglecting the left side of space. Because of these problems, she was totally disabled, needing help with activities such as dressing and showering. An MRI performed postoperatively showed a complete callosal section and the same hemispheric injuries noted in her preoperative scan (Figure), including the resected astrocytoma of the right frontal region, a right medial temporo-occipital lesion, and a left temporal lesion, but no evidence of new hemispheric damage.

About 1 year after her callosal section, she was evaluated at the University of Florida Cognitive and Memory Disorders Clinic (Gainesville). Cranial nerve examination revealed a dense left hemianopsia that did not abate when she gazed to the right side of space, suggesting deafferentation rather than inattention. During the examination, the patient had diminished spontaneous saccades to the left when compared with the right, suggesting an endogenously evoked directional akinesia of the eyes. When asked to look to the left (vs right), her leftward saccades were hypometric, suggesting that she also had an exogenously evoked akinesia or hypometria. When asked to watch the examiner's moving finger, she pursued fully to the right but broke her gaze before her eyes were fully to the left (directional impersistence). Her corneal reflex and left lower facial movement were both slightly reduced. The patient did not spontaneously move either her left arm or leg. When we asked her to move the extremities on her left side, no movements were observed. It appeared that she was densely hemiplegic, yet she made no trunk or face movements when instructed to move her left arm. This suggested that she was not attempting to move it, probably owing to an intentional deficit or akinesia. When the examiner moved her left arm to her right hemispace and encouraged her to move, the patient was able to move all of the joints of her left arm and was able to even offer some resistance, suggesting that part of her inability to move the left arm was a hemispatial limb akinesia, a form of motor neglect. Although she did have a spastic catch in her left lower extremity and an extensor plantar response on the left, suggesting a corticospinal injury, these signs were also noted prior to her callosal surgery. The patient could not report the presence of any sensory stimuli on the left side.

She was not aphasic but her speech was sparse and she used simple sentences. Her comprehension and repetition were excellent. She did have a reduction of her working memory, with a digit span of 4 forward. The patient knew the month, season, and year, but did not know the date or where she was being examined. When asked to recall 3 objects, she was immediately able to recall these objects, but after being distracted, she could recall none.

When asked to find the midpoint of lines that ranged in size from 7 to 10 in, she veered to the right. Her mean percent error (deviation from midline, divided by the size of the line, multiplied by 100) was 21.96% to the right. When given a line cancellation test that contained 18 lines distributed over a page, she only canceled 7 lines, and all of these lines were on the the right side of the page. When asked to draw intersecting pentagons, she drew 2 rectangles one on top of the other. Her map finding, however, was good, including the placement of California and Oregon on an outline map of the United States.

The patient appeared abulic, bradyphrenic, and bradykinetic. She had both motor (sustained eye closure) and cognitive impersistence. Examples of her cognitive impersistence include her performance on the Hopkins Verbal Learning Test, where the same 12 words are given 3 times. Almost all patients, including those with amnesia, improve the number of words recalled with each subsequent trial. In our patient’s first trial, she recalled 7, in the second trial, she recalled 5, and in the third trial, with the same words, she recalled only 3. Similarly, on the Controlled Word Association Test, where the patient is asked to name as many words as possible that begin with the letters F, A, and S, she produced 9 words that started with the letter F, 6 with the letter A, and 1 word with the letter S.

After callosal section, this patient developed a severe neglect syndrome, including spatial neglect. For example, on line bisections, she erred 21.96% to the right of the actual midline, and according to Mennemeier et al, normal sub-
Projects do not make errors of greater than 2%. She also demonstrated several forms of motor neglect, including hemispatial limb akinesia, directional akinesia, and directional impersistence of the eyes. There are several possible explanations of why sectioning of the corpus callosum induced neglect in this patient. Neglect has been reported with seizures and in the postictal state. Although this patient’s EEG did reveal widespread epileptic discharges, we do not think her neglect was related to seizures because she had this EEG pattern before her callosal section, and her neglect did not appear to be intermittent. After sectioning the corpus callosum, patients often have a tran-
sient akinetic mute state.10 This akinetic mutism is thought to be related to traction on the medial portions of both frontal lobes. Akinetic mutism may be a form of bilateral motor neglect and a unilateral neglect syndrome in humans has been reported with right-sided medial frontal lobe injuries.11 Ablation studies in old-world (Macaca) monkeys have confirmed the clinical observation that unilateral medial frontal lesions that include the cingulate gyrus may induce contralateral neglect.12 While it is possible that the neglect that developed in our patient after sectioning of the corpus callosum was related to injury of the medial right frontal lobe, our patient’s neglect persists, unlike the patients with a transient akinetic mutism following callosal section, suggesting that traction during surgery could not be the entire explanation of her neglect. Although there might have been some permanent medial damage induced by surgery, brain imaging performed after the surgery did not reveal any damage to the medial frontal lobe.

In the absence of hemispheric injury, an unusual form of spatial neglect has been reported in patients following callosal injury.13-15 When performing tasks such as line bisection, these patients had an ipsilateral bias such that when their right hand performed in left viewer-centered space, it deviated to the right, and when their left hand performed in right space, it deviated to the left. The spatial neglect our patient demonstrated is unlike that observed in these prior reports and is more typical of the neglect associated with right hemisphere lesions.

Our patient had her right hemisphere injury when she was a teenager, and younger people have greater brain plasticity than do older people. Thus, another possibility is that following the injury to her right hemisphere, she did not have neglect because the left hemisphere was able to compensate for and help activate the right hemisphere. The callosal section, however, interrupted the ability of the left hemisphere to help perform these functions. This compensation hypothesis has been supported by animal research.16 An experimental group of Macaca monkeys underwent a callosal section, while the control group had their corpus callosum intact. After the experimental animals recovered, both groups underwent hemispheric ablations that induced neglect. The experimental monkeys with the callosal section had more severe neglect than did the control animals, thereby providing support for the compensation model.

The cognitive impersistence demonstrated by our patient is an unusual sign and we could not find any prior references to this phenomena. Motor impersistence, however, also demonstrated by this patient, is often associated with neglect17 and right frontal lobe injury.18 Unfortunately, because we did not examine this patient for cognitive or motor impersistence before her callosal section, we cannot be certain of how the callosal section influenced these cognitive and motor intentional disorders.

Following this patient’s callosal section, she was also unable to use her left arm. In addition to sensory attentional deficits, patients with neglect might have motor intensional deficits, including limb akinesia or motor neglect.3 The mechanism of this motor neglect may be similar to that of sensory neglect. With her prior right hemisphere injury, she may have had mild or compensated intentional deficits, including limb hemispatial akinesia, directionolocular akinesia, and directionolocular impersistance, but her left hemisphere may have been helping to compensate for these deficits. Callosal section may have prevented the left hemisphere’s motor intentional systems from being able to activate the right hemisphere’s motor systems, and the latent limb and oculor motor intentional deficits became manifest.

Finally, this case has important pragmatic implications. Patients with lesions in areas of the brain known to be associated with neglect may have a greater risk for developing neglect with callosal section.

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